A Guide to Symptom Management in Palliative Care

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Yorkshire and Humber Palliative and End of Life Care Groups

A GUIDE TO SYMPTOM MANAGEMENT IN PALLIATIVE CARE

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INTRODUCTION

This guidance covers some of the commonest symptoms in cancer and advanced progressive disease. For the management of other symptoms not included here, including fatigue, cough, sweating, anorexia and cachexia please see an introductory palliative care text and refer to the other useful resources listed in the introduction.

Authorship

Health Education England working across Yorkshire and the Humber has sponsored the production of these symptom management guidelines which have been produced by the regional Palliative and End of Life Care Groups of Yorkshire and Humber. They were updated in March 2016 and reflect a consensus of opinion from specialists working in the field of palliative medicine in hospitals, hospices and in the community.

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Disclaimer

These guidelines are the property of the Yorkshire and Humber Palliative and End of Life Care Groups. It is intended that they be used by qualified medical and other healthcare professionals as an information resource, within the clinical context of each individual patient's needs. The groups take no responsibility for any consequences of any actions taken as a result of using these guidelines. Readers are strongly advised to ensure that they are acting in line with current accepted practice and legislation, as these may change. These include, but are not limited to, the NICE guidance on the prescription of opioids, the British National Formulary (BNF) and the Palliative Care Formulary (PCF). No legal liability is accepted for any errors in these guidelines, or for the misuse or misapplication of the advice presented here.

In difficult situations, please seek advice from your local Specialist Palliative Care service.

Useful Resources

Details are given here of selected widely used medicines. See also BNF sections on "Controlled Drugs" and "Prescribing in Palliative Care". Check the BNF for formulations, dose recommendations, side effects and contra-indications.

Other useful resources are:

- Local intranet guidelines
- The latest version of: "The Palliative Care formulary (PCF)." Twycross R, and Wilcock A, Radcliffe Medical Press Ltd and website www.palliativedrugs.com/
- www.evidence.nhs.uk
- NICE website, www.nice.org.uk/guidance.

- GMC guidelines, "Treatment and care towards the end of life: good practice in decision making", (2010), www.gmc-uk.org
- http://www.ncpc.org.uk/sites/default/files/How_Would_I_know.pdf

The Use of Medicines Beyond (Off-Label) and Without Marketing Authorisation

The use of medicines for off-label purposes is necessary when the clinical need cannot be met by the specifications of its marketing authorisations (MA), e.g. for an unauthorised indication, or in doses, preparations, patient population or route not covered by the MA. The recommendations within this symptom management guide include the off-label use of authorised medicines. These recommendations are based on current accepted palliative care practice in the UK. In practice, approximately 25% of medicines prescribed for palliative care patients are used off-label (e.g. when given by subcutaneous injection when only licensed for IM or IV use; for the treatment of nausea and vomiting when only licensed as an antipsychotic; or when mixing medicines in a syringe before administration by continuous infusion). Further information regarding off-label use of individual palliative care medicines can be found in the current version of the PCF.

Prescribing unauthorised medicines, or authorised medicines for off-label indications, may carry significant risks. The prescriber signing the prescription takes full responsibility. When prescribing medicines off-label, it has been suggested that the prescriber should: discuss with the patient and document in the patient's records

the reason why they are using the medicine off-label; where appropriate, gain informed consent from the patient; inform nurses and pharmacists to avoid misunderstandings where necessary; and give the patient a written leaflet where appropriate. A suitable leaflet may be downloaded from: https://www.britishpainsociety.org/static/uploads/resources/files/useofmeds_professional_final.pdf.

In practice, recording every unlicensed use may be impractical and gaining informed consent in every instance may lead to unnecessary anxiety for the patient or carer. Practitioners must follow their clinical judgment on the balance of potential burden and benefit and their own organisation's policy on the use of authorised medicines for off-label purposes.

Principles of Symptom Management

1. Remember to consider the 'whole patient'. Symptoms are rarely purely physical or purely psychological, and all symptoms and treatments impact on the patient, their family and friends.

2. Evaluate symptoms thoroughly. Consider potential causes and remember to consider causes other than the underlying condition. Consider the impact of the symptom on the patient's quality of life.

3. Effective communication is essential. Explain in simple terms and avoid medical jargon. Discuss treatment options with patients and their families, and involve them in the management plan.

4. Correct the correctable, as long as the treatment is practical and not overly burdensome. Remember non-drug treatments, e.g. palliative radiotherapy for metastatic bone pain.

5. Remember to consider non-pharmacological strategies to help relieve symptoms e.g. simple repositioning, or the use of a TENS machine may help pain; complementary therapies may help psychological distress. Although the evidence base for such treatments is not robust, some patients find them helpful.

6. When using drug treatments for persistent symptoms, give regularly and also 'as needed' (p.r.n.). Keep drug treatment as simple as possible.

7. Review regularly and adjust treatment.

8. Plan in advance. Good communication is essential in establishing patients' wishes for their future care and treatment. Patients may want to document their wishes – the Preferred Priorities for Care document (available from www.endoflifecareforadults.nhs.uk) or an Advance Decision to Refuse Treatment may be helpful.

9. Keep other staff informed.

10. Ask for help. Refer to local guidelines or speak to the local Specialist Palliative Care team (SPCT). Refer to GMC guidelines (see Useful Resources, page 4).

SECTION A: PRINCIPLES OF PAIN MANAGEMENT

1. Pain is common in advanced cancer and non-malignant conditions, and its management can be difficult.

2. Pain is a total, personal experience with physical, psychological, social and spiritual dimensions. Optimal pain management will be compromised if any of these aspects are neglected. Management requires a multidisciplinary approach.

3. Regular review of the pain, effect and side effect of analgesics and how the pain is affecting the patient/family is vital for good pain control.

4. Not all pain experienced by a patient with cancer is caused by the cancer itself. Often several pains coexist, and an accurate diagnosis of the cause as well as the type of pain and severity of each pain is necessary to enable effective pain management. Analgesic options will be determined by the specific cause, type and severity of pain. Previous exposure to analgesics (efficacy and side effects) will also determine the type and strength of analgesics used.

5. Principles of use of analgesia

a. Analgesics can be divided into three classes:

- Non-opioid (simple analgesics), e.g. paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs)
- Opioids (weak and strong)
- Adjuvants (co-analgesics)

b. Medicines from different classes are used alone or in combination according to the type of pain and response to treatment. Two medicines of the same class (e.g. NSAIDs) should generally not be given concurrently; however, immediate release and sustained release opioids may be prescribed together.

c. Morphine sulphate orally (or diamorphine/ morphine subcutaneously) is the most commonly used opioid in advanced cancer and other end-stage conditions, although non-opioids (e.g. paracetamol), a weak opioid and/ or an adjuvant may suffice. Alternative opioids may be required in patients with renal and liver impairment or in those who develop side effects (seek specialist advice).

c. Some pains are only partially opioid-responsive. These include treatment related pains such as chemotherapy-induced neuropathy and pains unrelated to the underlying illness, such as tension headache, post-herpetic pain, muscle spasms, nerve damage/compression, bone pain, visceral distension/spasms, tenesmoid pain and activity provoked pain. These may require other measures including adjuvants, nerve blockade or oncological treatments if cancer related.

d. In general, successful relief of pain in palliative care patients requires:

- Careful assessment and re-assessment
- Consideration of the "WHO Method for Relief of Cancer Pain" which summarises the principles of analgesic use (Figure 1)

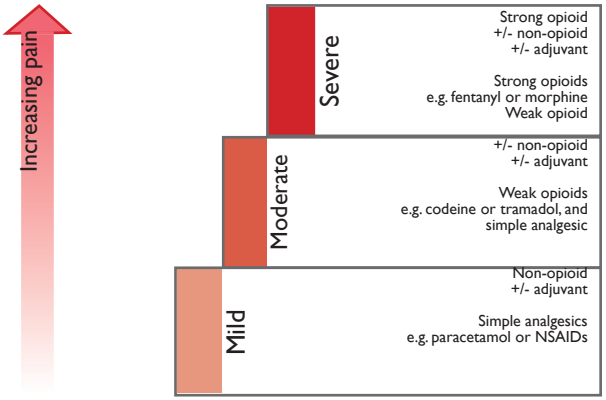

Figure 1: Three-step WHO "ladder" for cancer pain relief in adults

- Appropriate time interval between doses.
- Sufficient dose to prevent return of pain before next dose is due.
- Willingness to give strong opioids when other analgesics fail.
- Early consideration of adjuvants and non-pharmacological approaches.
- Regular review and assessment of pain control and use of as required (p.r.n.) medication. If patients are requiring several p.r.n. doses a day, assess the effect and side effects of these (if these fit with the drug's pharmacokinetics), and whether this is due to inadequately controlled background pain or the presence of breakthrough (episodic) pain.
- Appropriate communication with the patient: explanation, asking about concerns and providing both verbal and written information where necessary on drug treatment (see section C, Communicating about opioids).
- Referral for anaesthetic interventions as necessary.

- If parenteral opioids are required, a continuous subcutaneous infusion (CSCI) by a syringe pump and/or p.r.n. subcutaneous (SC) injections should be used.

SECTION B: ASSESSMENT AND REVIEW

To manage pain effectively it is important to assess the:

1. Cause of pain.

Consider other causes/exacerbators of pain (e.g. psychological, spiritual and social) and perform a full holistic assessment.

a. Investigate appropriately, e.g. X-ray for pathological fracture; ultrasound or CT scan for deep soft tissue tumours; urgent MRI for suspected spinal cord compression.

b. Remember common non-malignant causes, e.g. arthritis, tension headache and infections, including oral candidiasis.

c. In advanced, progressive disease there are usually multiple causes of pain and a management plan will be needed for each of these.

2. Type of pain: acute vs. chronic; nociceptive vs. neuropathic vs. inflammatory vs. visceral pain; episodic: breakthrough and incident pain.

3. Severity of pain. Use a combination of clinical assessments, e.g. facial expressions, groaning,

the ability to move, the timing of pain, the number of sites and the patient's own perception, e.g. pain-rating scales.

4. Remember: Ask what helps? What makes it worse? Explore the effect of pain and analgesics (including side effects). Review and re-review as pain/analgesic requirements may change.

Which Analgesic?

The principles governing analgesic use are summarised in the WHO Method for Relief of Cancer Pain:

- **By mouth,** where possible
- **By the clock:** Regular, as well as p.r.n. dose
- **By the ladder:** (Figure 1)
    - o After assessing the severity of pain, the analgesic ladder can be used to identify appropriate analgesics for the level of pain.
    - o The patient should be reassessed and analgesia administered in a step-wise manner working up the ladder until the patient's pain is managed.
    - o Similarly, if the severity of pain is reduced, a patient's level of analgesics should move back down the ladder, eventually stopping treatment when pain resolves.
    - o Alternative analgesia and adjuvants or non-pharmacological interventions should be considered at each level of the analgesic ladder.
- **Individual dose titration:** Titrate dose against effect, with no rigid upper limit for most opioids except buprenorphine, codeine and tramadol.

SECTION C: RECOMMENDED MEDICINES

1. Opioid analgesics

Weak Opioids

- Include codeine, dihydrocodeine and tramadol
- Co-codamol is available in three strengths containing paracetamol and either 8mg, 15mg or 30mg of codeine. In elderly or frail patients a lower strength may be required.
- Codeine is a pro-drug of morphine. Its analgesic effect is via conversion to morphine, which varies between patients and there is a small proportion of the population in whom codeine is ineffective.

Strong opioids

- Strong opioids include morphine, diamorphine, oxycodone, fentanyl, alfentanil, hydromorphone, buprenorphine, and methadone (specialist use only).

Opioid side effects

These include:

- Constipation (very common, always prescribe a laxative).
- Nausea and vomiting (always prescribe a p.r.n. antiemetic).
- Drowsiness (dose-related and often temporary).
- Confusion, hallucinations and delirium (may need a dose reduction, if pain free, or change in opioid).
- Respiratory depression (rarely a problem if titrated correctly). Both respiratory rate and oxygen saturations will be decreased if opioid-induced.
- Neither tolerance nor addiction are significant problems in patients at the end of life.

General Principles

1. Immediate and modified (slow) release preparations are available.

2. All patients taking regular analgesics should also have analgesics prescribed for 'breakthrough pain' to take p.r.n.

3. p.r.n. immediate release opioids should be **individually** titrated. Commonly this is 1/6 of the total daily dose, but a range may be appropriate (e.g. 1/6 to 1/10). For a patient on 30mg slow release morphine sulphate b.d. 1/6 of their total 24 hour morphine dose would be 10mg immediate release morphine.
   Do not make changes to the p.r.n. dose if this is effective for the patient, irrespective of the background dose.

4. Maximum frequency and dose of p.r.n. opioids in 24 hours should be clearly stated.

5. Prescribe opioids in mg rather than mL as differing strengths are available.

6. Prescribe regular laxatives and p.r.n. anti-emetics.

7. Discuss side effects of opioids with the patient, including the potential impact on driving (see DVLA guidance - https://www.gov.uk/current-medical-guidelines-dvla-guidance-for-professionals).

8. When using opioid analgesics, if the pain is inadequately controlled and opioid responsive, then the background dose of opioids should

be increased, taking the p.r.n. requirements into account, after assessment of the effect and side effects of these.

9. Halve the usual starting doses if the patient is elderly or frail.

10. Some analgesics (including morphine) may accumulate in renal or hepatic impairment and specialist advice may be required. Careful individual tailoring of opioid dose is also required in patients with respiratory failure.

11. It is advisable to seek specialist palliative care advice regarding patients receiving higher doses of opioids (>120mg/day oral morphine equivalent), especially when undertaking conversions to alternative drugs or routes of administration.

Communicating About Opioids [NICE CG140]

- When offering pain treatment with strong opioids to a patient, ask them about their concerns such as:
    - addiction
    - tolerance
    - side effects
    - fears that treatment implies dying

- Provide verbal and written information on strong opioid treatment to patients and carers, including:
    - When and why strong opioids are used to treat pain
    - That opioids are not addictive
    - How effective they are likely to be

- How, when and how often to take strong opioids (for background and breakthrough pain)
- How long pain relief should last
- Side effects and signs of toxicity
- Safe storage
- Follow-up and further prescribing
- Information on who to contact out of hours

- Offer patients access to frequent review of pain control and side effects

1.1 Oral Preparations

1.1.1 Morphine sulphate

Formulations available
Immediate release tablets and liquids would be expected to be effective after 20-30 minutes and to last up to 4 hours. Examples include Oramorph® solution (10mg/5ml, 20mg/1ml) and Sevredol® tablets (morphine sulphate immediate release tablets - 10mg, 20mg, 50mg).

Modified/slow release tablets, granules and capsules would be expected to be effective after 4 hours and to last for 12 hours. Examples include MST Continus® tablets and suspension sachets, and Zomorph® capsules.

Starting regimen
- It is acceptable in opioid-naïve patients to either start weak opioids, e.g. codeine, or low dose strong opioids.
- If the optimal dose of weak opioid with or without paracetamol and/or an adjuvant drug does not control the pain, the patient should be changed

to morphine at a dose which is equivalent to the dose of the weak opioid that they are taking (see Appendix 1 for conversions). The weak opioid must then be stopped. E.g. a patient taking 60mg of codeine phosphate q.d.s. regularly, could be commenced on slow release morphine sulphate (e.g. MST®, Zomorph®) 10mg b.d. with immediate release morphine for breakthrough pain.

- If the pain is intermittent or there are concerns about opioid sensitivity, commence immediate release morphine:

- 2mg to 5mg 4 hourly p.r.n.

- 1mg to 2mg 4 hourly p.r.n. in the frail or elderly

Reduce dose in renal failure, or consider an alternative opioid (seek specialist advice).

- Once a stable dose is achieved it is usual to convert to modified release preparations, e.g. a patient on 5mg oral morphine immediate release (e.g.Oramorph®) 4-6 hourly receives a total of 20mg morphine in 24 hours. This is equivalent to 10mg 12 hourly of morphine sulphate (modified release) tablets, e.g. MST®, Zomorph®.

Patients being initiated on morphine by either method should have their doses reviewed every 24 hours. If the pain is inadequately controlled and is thought to be responsive to opioids then the background dose of opioids should be increased, taking the p.r.n. requirements into account. It is not advisable to increase the 24 hour dose by greater than 30%.

All patients being titrated on morphine should be monitored for side effects and signs of CNS toxicity (confusion, drowsiness, hallucinations, myoclonic jerks). If the patient has moderate to severe renal impairment, morphine and its metabolites will accumulate and specialist advice may be required regarding alternative opioids.

Breakthrough pain
All patients on modified release morphine should have immediate release morphine available p.r.n. for breakthrough pain.

1.1.2 Oxycodone

Oxycodone is a strong opioid with a similar dosing schedule to morphine. It is a useful second line strong opioid for patients who have not tolerated morphine and may be first line in moderate renal impairment. Caution is needed in severe hepatic impairment. Oral oxycodone is 1.5 to 2 times more potent than oral morphine. Consult a dose conversion chart when converting to oxycodone or ask advice from your local palliative care team or pharmacy.

Formulations available
Oxycodone is available as immediate release (e.g. OxyNorm®) with a duration of action of 4-6 hours, or modified/slow release (e.g. OxyContin®) with a duration of action of 12 hours.

Breakthrough pain
Immediate release oxycodone should be available p.r.n., at a dose which is usually about 1/6 of the 24 hour oxycodone dose.

1.2 Parenteral preparations

This section contains information needed for prescribing continuous subcutaneous infusions (CSCI) via syringe pump. Syringe pumps are indicated if the patient is unable to take oral medication or there are concerns about absorption.

1.2.1 Diamorphine and morphine injections

Both diamorphine and morphine sulphate can be given p.r.n. subcutaneously (SC) with a duration of action of up to 4 hours. Alternatively they can be given as a CSCI via a portable syringe pump.

In an opioid naïve patient, start with morphine sulphate or diamorphine, between 1mg to 2.5mg SC p.r.n. or between 5mg and 10mg morphine or diamorphine over 24 hours as a CSCI.

Compared to oral morphine, parenteral morphine is about 2-3 times more potent and parenteral diamorphine is about 3 times more potent, although there is variability between individuals (refer to your local conversion policy).

For example, to change a patient from oral morphine to a CSCI of diamorphine, divide the total 24 hour dose of oral morphine by three, e.g. if a patient is on MST 30mg b.d., they will require 20mg subcutaneous diamorphine over 24 hours. As there is inter-individual variability, reassessment of effect and side effects is recommended after 24 hours.

It is extremely important that p.r.n. analgesia is prescribed. Usually this is 1/6 of the total 24 hour opioid dose, e.g. in the above example, the SC p.r.n. dose would be between 2.5mg and 5mg diamorphine.

Start with 2.5mg diamorphine which might need adjustment, depending on effect and side effects.

1.2.2 Oxycodone injection

Patients on oral oxycodone can be converted to a subcutaneous infusion of parenteral oxycodone. To convert to subcutaneous oxycodone from oral oxycodone, divide the total daily dose of oral oxycodone by two. As there is inter-individual variability, reassessment of effect and side effects is recommended after 24 hours. As discussed above, it is extremely important that p.r.n. analgesia is prescribed.

Note: There are two concentrations of parenteral oxycodone available: 10mg/ml and 50mg/ml.

1.3 Transdermal preparations

Transdermal preparations are suitable for patients with chronic pain already stabilised on other opioids. They may be useful in patients with poor compliance with oral opioids or swallowing/absorption problems. They should not be started in unstable pain or in the last days of life due to their long titration period and duration of action. Some patients may experience fewer adverse effects than with oral morphine. Both fentanyl and buprenorphine are safer than morphine in patients with renal failure.

N.B. All patients using transdermal patches should also be prescribed an immediate release preparation for breakthrough pain, the dose of which is dependent on the patch strength (See conversion tables or local guidance for details).

Transdermal fentanyl patches are available in 12, 25, 50, 75 and 100 microgram per hour strengths and are applied every 72 hours.

Transdermal buprenorphine patches are available as:

- Low dose patches in 5, 10, 20 micrograms per hour strengths (BuTrans®) and are applied every 7 days. These may be helpful in patients with poor compliance who require a low dose opioid.

- Higher strength patches in 35, 52.5, 70 micrograms per hour (Transtec®) and are applied every 96 hours. They are changed twice a week.

Consult a dose conversion chart (see local guidelines and Appendix1) when starting transdermal opioids or ask for advice from your local palliative care team or pharmacist.

1.4 Other routes of administration of strong opioids

Formulations of sublingual, buccal and nasal fentanyl are available and may be advised in specific situations by specialist teams.

1.5 What if opioids do not work?

a. Are opioids the analgesic of choice?

Not all pain is opioid responsive. Consider its aetiology.

Palliative radiotherapy is helpful for bone metastasis, and can be given as a single treatment. In certain patients a nerve block will help, e.g. coeliac plexus block in pancreatic pain. Discuss with palliative care or chronic pain specialists.

b. Is the dose high enough?

If there is a partial response or inadequate duration of pain relief, i.e. if pain returns less than 4 hours after immediate release oral morphine or less than 12 hours after modified release morphine, and there are no side-effects, increase the dose by 30% increments rather than shortening the interval between doses. Remember to check that the p.r.n. dose prescribed is adequate for the background dose.

c. Is the drug being absorbed?

If there is uncontrolled vomiting, dysphagia or high stoma output, consider alternative routes of delivery, e.g. subcutaneous, intravenous, transdermal.

d. Is pain breaking through with movement or painful procedures?

Identify and minimise provoking factors. Consider pre-emptive doses of immediate release opioid; consider NSAIDs. Discuss with palliative care team.

e. Are adjuvants required?

Please see next section for indications.

f. Who might be able to help?

Do not be afraid to ask a more experienced colleague for help. Your hospital palliative care team, local hospice or community palliative care team will gladly offer advice.

2. Adjuvants

Choice of adjuvant analgesic will be determined by the aetiology of the pain.

2.1 Medicines for cancer induced bone pain

Consider NSAIDs, bisphosphonates, palliative radiotherapy and corticosteroids, as well as opioids and medicines for neuropathic pain (see section 2.2).

2.2 Medicines for neuropathic pain

The decision to use an antidepressant or an anticonvulsant depends on a patient's symptoms and the adverse effect profile (anti-cholinergic side-effects with amitriptyline include dry mouth, urinary hesitancy, postural hypotension and constipation. Sedation, dizziness and gastro-intestinal effects occur with gabapentin or pregabalin). Remember to consider the patient's comorbidities when prescribing.
Refer to NICE guidelines CG173: Neuropathic pain – pharmacological management: the pharmacological management of neuropathic pain in adults in non-specialist settings.

2.2.1 Antidepressants

Start with low dose, e.g. amitriptyline 10mg at night, titrating gradually every 2-5 days, if adverse effects allow, to 75mg at night (lower than usual antidepressant doses).

2.2.2 Anticonvulsants

Titration is often slower than stated in the BNF, with particular caution needed in frail and elderly patients. Start with the lowest dose. Use with caution and dose reduce in renal impairment and seek advice if necessary.

Gabapentin	Start 100mg t.d.s. slowly titrate assessing efficacy/ adverse effects; maximum dose 600mg q.d.s.

Pregabalin Start 25 to 75mg b.d.; slowly titrate assessing efficacy/adverse effects; maximum dose 300mg b.d.

In addition, for nerve root compression consider a short course of 4 to 8mg dexamethasone, NSAIDs, palliative radiotherapy, and pain team interventions.

2.3 Medicines for pain due to raised intracranial pressure

Dexamethasone is the corticosteroid of choice with high anti-inflammatory potency, high solubility and low mineralocorticoid effect (less salt and fluid retention).

Use 4 to 8mg unless severe symptoms or risk of coning, in which case use 16mg o.d. Titrate down to lowest effective dose, and use for shortest possible time. Taper the dose slowly when stopping (not usually necessary if duration of treatment less than two weeks). Prescribe doses to be given in the morning to avoid causing insomnia. Remember the risk of hyperglycaemia.

Note: 1mg Dexamethasone = 7mg Prednisolone

2.4 Medicines for other pain

Management depends on the aetiology of the pain; thorough assessment is vital.

Painful skeletal muscle spasms

Diazepam 2 to 5mg, once at night (or b.d./t.d.s.)

Baclofen 5mg t.d.s.

Liver capsule pain
Consider trial of NSAIDs or dexamethasone between 4 and 8mg o.d.

Musculoskeletal pain
Consider NSAIDs (oral or topical), or transcutaneous electrical nerve stimulation (TENS) machine.

Intestinal colic
Anti-spasmodics; hyoscine butylbromide 20mg SC.
Also see Intestinal Obstruction section, page 33.

Pelvic pain
Consider NSAIDS or corticosteroids, and antispasmodics for colic.

2.5 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Most patients with cancer/advanced progressive disease have risk factors for significant gastrointestinal adverse effects, therefore consider use of an H2-receptor antagonist or a proton-pump inhibitor alongside NSAIDs. Use NSAIDs with caution in patients with renal impairment, uncontrolled hypertension or heart failure. Balance the short and long term risks and benefits.

Ibuprofen tablets	400mg t.d.s
Naproxen tablets	250 to 500mg b.d.

2.6 Other medicines

A wide variety of other medicines can be used as analgesics, e.g. ketamine, methadone, lidocaine plasters, Targinact® and tapentadol. Their use should be guided by specialists.

OPIOID ANALGESIC EQUIVALENCES

General Principles

a. LOCAL ORGANISATIONAL OPIOID CONVERSION CHARTS for opioid use in palliative care MUST be used in preference to these tables.

b. If there is any uncertainty regarding the safe prescribing of opioids seek specialist advice before doing so.

c. It is advisable to double check calculations and document method used in the patient record, including for appropriate p.r.n. opioid.

d. Clinical judgement must also be applied, considering: underlying clinical situation; comorbidity and concomitant medicines; nature of pain and its opioid responsiveness; toxicity of current opioid; previous opioid doses and adherence; rapidity of opioid escalation; reason for switching - if pain is controlled, switching due to adverse effects or convenience is usually less problematic than switching if the pain is uncontrolled (seek specialist advice).

e. In view of incomplete cross tolerance, caution is needed when converting between opioids. Start with the most conservative dose.

f. Larger doses of opioid often require an empirical decrease in the dose of the replacement opioid and re-titration. For doses greater than 120mg

oral morphine equivalence a day it is advisable to seek advice. Specialist advice is strongly recommended for doses greater than 200mg oral morphine equivalence a day.

g. Analgesic review and monitoring for adverse effects, including consideration of patient's place of care, need to be in place, documented in the patient record and communicated.

These tables should only be used in the context of these guidelines as a whole, and used alongside the summary key principles outlined above.

Step 2 ("weak") opioids - dose conversion to oral morphine sulphate N.B. Some people cannot efficiently metabolise codeine or tramadol to the active metabolite and therefore they may require a lower dose of morphine			
Oral "Weak" opioid	**Total MAX daily dose**	**Conversion factor**	**Approximate 24 hour oral morphine sulphate dose equivalence**
Oral codeine phosphate	240mg/day	÷ 10	24mg/day
Oral dihydrocodeine	240mg/day	÷ 10	24mg/day
Tramadol hydrochloride	400mg/day	÷ 10	40mg/day

TRANSDERMAL FENTANYL

Comparative doses based on dose conversion ratio of between 100 to 150:1 (approximated). Changed every 72 hours. If possible, patients should not be switched between brands when on stable dose.

Start with the most conservative dose conversion, reassess and titrate if needed. Use local organisational opioid conversion charts in preference to these tables. Seek specialist advice for higher doses or if you are uncertain of the conversion.

Fentanyl patches micrograms/ hr	**24 – hourly oral morphine sulphate dose**	**4-hourly and breakthrough oral morphine sulphate dose (rounded to practical amounts)**
12	30 to 45mg	5 to 10mg
25	60 to 90mg	10 to 15mg
37	90 to 135mg	15 to 20mg
50	120 to 190mg	20 to 30mg
62	150 to 220mg	25 to 35mg
75	180 to 310mg	30 to 45mg

These tables should only be used in the context of these guidelines as a whole, and used alongside the summary key principles outlined above and local guidelines.

TRANSDERMAL BUPRENORPHINE

Table for converting from morphine to Buprenorphine Comparative doses based on dose conversion ratio of between 75 to 115:1 (approximated). Start with the most conservative dose conversion, reassess and titrate if needed. Use local organisational opioid conversion charts in preference to these tables. Seek specialist advice for higher doses or if you are uncertain of the conversion.

Buprenorphine patches micrograms/hr	**Approximate 24–hourly oral morphine sulphate dose equivalence**	**Approximate 4-hourly and breakthrough oral morphine sulphate dose**
BuTrans® - **changed weekly**		
5	10 to 15mg	1 to 2mg
10	20 to 30mg	3 to 5mg
20	35 to 55mg	5 to 10mg
Transtec® - **changed twice weekly**		
35	60 to 95mg	10 to 15mg
52.5	95 to 145mg	15 to 20mg
70	125 to 190mg	20 to 30mg

These tables should only be used in the context of these guidelines as a whole, and used alongside the summary key principles outlined above and local guidelines.

NAUSEA AND VOMITING

- It is important to fully assess and consider all possible causes, including those which may require specific treatments rather than an antiemetic alone (e.g. hypercalcaemia, gastritis, oral candidiasis).

- Causes can be multifactorial.

- Prescribe drugs regularly as well as p.r.n.

- If there is significant nausea and/or vomiting, the oral route may be temporarily ineffective and parenteral anti-emetics may be required. The subcutaneous route is preferred unless the intravenous route is required for another purpose.

- Consider disease specific cautions when prescribing:

    - Cyclizine may worsen heart failure.

    - Centrally acting anti-dopaminergic drugs such as metoclopramide, haloperidol and levomepromazine may worsen Parkinsonian symptoms. Consider using domperidone or a 5HT3 antagonist in Parkinson's disease.

    - Cyclizine and other antimuscarinic drugs block the final common pathway through which metoclopramide acts, therefore concurrent administration should be avoided.

- Cyclizine and hyoscine butylbromide (Buscopan®) may crystallize when mixed in a syringe pump and should only be used together on specialist advice.

- If initial advice in the Drug Management Table (page 76) is not effective, contact your local Palliative Care Team.

The European Medicines Agency's Committee on Medicinal Products for Human Use recommended key changes to the licensed use of metoclopramide and domperidone. They concluded that the benefit of these drugs outweighs the risk only when used short-term for nausea and vomiting and not as a prokinetic. If the use of metoclopramide or domperidone is being considered above the MHRA recommended dose of 30mg daily or for more than one week for domperidone and 5 days for metoclopramide, seek specialist advice. Avoid/seek advice before using domperidone for anyone known to have heart disease/ conduction defects - ECG monitoring may be advised for some patients. Avoid metoclopramide in people with a history of extrapyramidal disorders and tardive dyskinesia. In palliative care, off-label use is recognised as standard practice and recommended cautions to the licensed use of the prokinetics should not necessarily change practice.

RECOMMENDED DRUG MANAGEMENT OF NAUSEA AND VOMITING

CAUSE	FIRST-LINE DRUG	STAT DOSE (PO or SC)	24 HR RANGE
Gastric stasis and irritation	Domperidone or metoclopramide +/- proton pump inhibitor/ H2 receptor antagonist	10mg PO 10mg PO or SC	30 to 60mg PO or SC
Bowel obstruction WITHOUT colic	Metoclopramide	10mg SC (Only use SC)	30 to 60mg SC (Only use SC)
Bowel obstruction WITH colic	Cyclizine +/- haloperidol +/- hyoscine butylbromide (Buscopan®) NB: cyclizine and buscopan can be incompatible	50mg SC 1mg SC 20mg SC (Only use SC)	150mg SC 1 to 5mg SC 60 to 120mg SC (Only use SC)
Chemical e.g. •drugs •hypercalcaemia •uraemia	Haloperidol	500 micrograms PO or SC	1 to 5mg PO or SC
Raised intracranial pressure	Dexamethasone +/-cyclizine	8 to16mg 50mg PO or SC	8 to 16mg 100 to 150mg PO/SC
Motion	Hyoscine hydrobromide OR Cyclizine	300 micrograms sublingual 400 micrograms SC 50mg	300 micrograms SL q.d.s. 800 to 1200 micrograms SC 150mg PO or SC
2nd line or Multifactorial	Levomepromazine	6.25mg	6.25 to 12.5mg PO or SC

INTESTINAL OBSTRUCTION IN ADVANCED CANCER

Introduction

Intestinal obstruction in advanced cancer is the interrupted passage of food and fluids through the gastrointestinal tract due to mechanical or functional obstruction. It could be partial, complete, or intermittent, at single or multiple sites. The incidence of intestinal obstruction in advanced cancer is between 3% and 6%. It occurs more often in ovarian and bowel cancers.

Clinical Features

Symptoms depend on the level, type and duration of intestinal obstruction and may include any or all of the following:

- Nausea: often postprandial, intermittent and relieved by vomiting undigested food
- Vomiting: may be faeculent (irrespective of the site of obstruction)
- Dull aching pain due to tumour mass and/or nerve infiltration
- Colicky pain and altered bowel sounds. Often due to mechanical obstruction
- Abdominal distension, although this may be absent in high obstruction
- Paradoxical diarrhoea and/or constipation
- Other symptoms include anorexia, dry mouth and dehydration

Diagnosis

- History and physical examination are the most useful.
- Contrast radiography may help define site and extent of obstruction. CT scan assists in choice of surgical intervention. Abdominal X-rays (supine and erect) may

help but "normal appearances" do not exclude bowel obstruction.
- An important differential diagnosis is constipation due to faecal impaction which may mimic, or co-exist with and complicate, intestinal obstruction.
- Passage of flatus stops in complete obstruction and therefore passage of flatus or stools argues against this.

Management

All patients will require symptom management that is specific to the individual and based on the aims of treatment as well as prognosis. Surgical intervention should also be considered early in selected cases.

Surgical Management

Palliative surgery is a reasonable option for some patients. However, selecting patients who are likely to benefit from a surgical procedure (e.g. bowel resection or by-pass +/- stoma formation) is difficult. These decisions are best made with an experienced surgical colleague and careful discussion with the patient. Patients likely to benefit are those with no other life-threatening disease and single-site obstruction. Other factors to consider include patient performance and functional status, prognosis (ascites is a poor predictor of outcome), co-morbidity, nutritional status and options for further treatment such as chemotherapy.

Medical Symptom Management

When surgical approaches are inappropriate or not possible, symptomatic palliative treatment aimed at reducing symptoms and providing the highest possible quality of life becomes the main priority. Good symptom management can usually be achieved and greatly improves quality of life.

General measures include:

- Mouth care.
- Small amounts of oral fluids and food as desired.
- NG tube: this is indicated while surgery is being considered or as a short-term intervention but is rarely appropriate for long-term management. An NG tube may occasionally be used as a venting mechanism to relieve vomiting in gastric outlet or high small bowel obstruction.

Pharmacological measures for symptoms
Medication should generally be given by subcutaneous injection or continuous subcutaneous infusion (CSCI).

a. Nausea and vomiting
- Set realistic goals. Nausea can usually be reduced significantly but vomiting may continue once or twice daily
- Give anti-emetics parenterally and regularly. Subcutaneous infusion is often helpful (see nausea and vomiting section, page 30)
- Anti-secretory drugs. These include hyoscine butylbromide, and octreotide (used under the guidance of a specialist).

b. Pain
Colicky pain
- Stop stimulant laxatives and prokinetic drugs, e.g. metoclopramide, in complete obstruction
- Use antispasmodics (hyoscine butylbromide, 60 to 120mg/24 hours by CSCI)

Dull aching pain
- Diamorphine or morphine subcutaneously (if helpful consider starting a CSCI)

Pain from tumour mass

- Consider dexamethasone/chemotherapy/ radiotherapy to reduce tumour/peri-tumour oedema (under specialist guidance)

c. Constipation

Examine lower rectum or stoma for faecal impaction, if safe and appropriate to do so.

For partial obstruction, use laxatives (softeners) with caution.

d. Ongoing nutrition and hydration

- IV fluids and total parenteral nutrition (TPN) are rarely appropriate in advanced cancer. SC fluids may be used for thirst; usually give 1L/24 hours.
- Oral intake of food and drink can continue for the patient's enjoyment and is often surprisingly well tolerated - the patient will decide if the risk of vomiting outweighs the pleasure of eating.

Note: Patients with a high obstruction without other life-threatening complications require special consideration regarding symptom management, hydration and nutrition, e.g. venting gastrostomy, subcutaneous fluids. TPN may be considered in individual cases.

CONSTIPATION

Constipation is very common in palliative care patients due to a combination of factors including immobility, reduced food and fluid intake, medication, bowel pathology and sometimes hypercalcaemia. Diagnosis is usually made on the basis of a history of decreased frequency of bowel movements, the passage of small hard faeces and the need to strain. Constipation can present with overflow diarrhoea. Abdominal X-ray is rarely required. Consider patient education and information about the causes of constipation, increasing fluid intake and making appropriate dietary changes to help improve symptoms.

Guidelines on the use of laxatives in constipation

- There is limited research for the management of constipation in palliative care patients and a lack of evidence to support a particular laxative regimen.

- Patient preference regarding laxative formulation (tablet, liquid, volume required), palatability and drug tolerability (flatulence, colic) can impact greatly on adherence and therefore patient views should be sought.

- Assess the cause and treat where possible. Most patients on regular opioids will require laxatives.

- A combination of stool softener and stimulant laxative is usually required.

- Examples of stool softeners include docusate, poloxamer, lactulose, Movicol® and magnesium salts.

- Examples of stimulant laxatives include senna, bisacodyl, sodium picosulphate.

- Local units may have their own guidelines on first line laxatives.

- Review laxatives every 2 days and titrate as required.

- Avoid stimulant laxatives if colic is present. If faecal leakage occurs consider reducing the dose of the softener.

- Lactulose may cause significant flatulence and bloating.

- In complete bowel obstruction, do not prescribe laxatives without seeking advice.

- If patients are managing well on their laxative regimen, there is no need to change laxatives.

- If bowels have not moved in 3 days, do a rectal examination if safe and appropriate to do so, and follow local guidelines on rectal measures.

Seek advice from your local specialist palliative care team regarding opioid-induced constipation resistant to optimal laxative regimens. Some opioids, e.g. fentanyl or buprenorphine are potentially less constipating. Also, peripherally acting opioid antagonists could be considered, e.g. subcutaneous methylnaltrexone, or combination preparations e.g. Targinact® (oxycodone and naloxone) or oral preparation Naloxegol®.

BREATHLESSNESS

Definition: an uncomfortable awareness of breathing. Breathlessness occurs very commonly in advanced cancer, and in cardiorespiratory and neurological diseases. Look for reversible causes as listed below.

Sudden onset breathlessness

Possible cause	Consider
Asthma	Bronchodilators, corticosteroids, physiotherapy
Pulmonary oedema	Diuretics, morphine
Pneumonia	Antibiotics, physiotherapy
Pulmonary embolism	Anticoagulants, morphine
Pneumothorax	Chest drainage

Breathlessness arising over several days

Possible cause	Consider
Exacerbation of COPD	Antibiotics, bronchodilators, corticosteroids
Pneumonia	Antibiotics, physiotherapy
Bronchial obstruction by tumour	Dexamethasone16mg o.d. early radiotherapy (RT), laser or stents
Superior vena caval obstruction	Dexamethasone16mg o.d. Urgent stenting

Breathlessness of more gradual onset

Possible cause	Consider
Congestive cardiac failure	Diuretics, digoxin, ACE inhibitors
Anaemia	If chronic, this is unlikely to be the major cause of breathlessness. Transfusion may help if Hb<80g/l. Oral iron is ineffective in chronic normochromic normocytic anaemia
Pleural effusion	Pleural aspiration and follow with pleurodesis if appropriate. These procedures may be distressing for frail patients.
Pulmonary fibrosis	Possible if history of cytotoxics (esp.bleomycin), or lung radiotherapy
Ascites	Paracentesis if appropriate.
Primary/secondary carcinoma lung	Resection, RT or chemotherapy as appropriate
Carcinomatous lymphangitis	Dexamethasone 8 to 12mg o.m. Stop if not effective within one week. Bronchodilators may help

Palliative management where there are no reversible causes

- Breathlessness is frightening for the patient, family and staff.
- Reassurance and explanation are vital parts of the treatment whatever the cause.
- Modification of lifestyle, breathing retraining, relaxation and tailored exercise may be beneficial if instituted early enough and should be provided for all breathless patients as tolerated.
- Consider referral to physiotherapist or occupational therapist.
- A portable/table fan directed onto the face.
- Good oral care is important if mouth breathing.
- Humidified oxygen may help acute breathlessness only in the presence of significant hypoxaemia. An exception to this rule is people with COPD where they may get benefit for breathlessness even with mild hypoxaemia. Use a trial of oxygen alongside other measures. Review regularly.
- Long term oxygen therapy for chronic respiratory illness should only be instigated by respiratory physicians.
- Most patients requiring palliation for breathlessness will not benefit from oxygen therapy (unless they are significantly hypoxaemic). Measurement of oxygen saturation levels using a pulse oximeter may aid decision making in assessing whether or not oxygen will be of benefit.

Medicines to consider
All medicines for symptomatic relief of breathlessness are respiratory sedatives. When prescribed, their use should be monitored carefully. In the context of distressing breathlessness in the terminal stages of illness the benefits usually outweigh the risks.

Opioids
Oral morphine sulphate modified release 5 to 10mg b.d. (with concurrent prescription of a laxative). Titrate by 5 to 10mg b.d. every 7 days until side-effects or a total daily dose of 30mg is reached.

Alternatively, if there is concern about fluctuating renal function, oral morphine (immediate release) may be given as 2.5mg up to 4 hourly and converted to modified release if tolerated.

If the patient is already taking a strong opioid for analgesia contact palliative care team for advice.

Benzodiazepines
Lorazepam 500 micrograms to 1mg SL may give rapid relief during panic attacks.

If anxiety appears to be a significant driver for the breathlessness, then try an anxiolytic anti-depressant, e.g. mirtazapine 15 to 30mg nocte, or citalopram 10 to 20mg nocte.

Midazolam 2.5mg SC may benefit patients who cannot tolerate the oral/sublingual route. These medicines can be continued in the terminal phase. See section on 'Last Days of Life' (page 61).

DELIRIUM

Delirium is extremely common in patients with advanced disease. It is a source of increased morbidity and distress and interferes with the ability to communicate effectively at the end of life.
It is often unrecognised or treated inappropriately and can be misdiagnosed as dementia, depression, anxiety or psychosis.

Clinical features

a. Disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.

b. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia.

c. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.

d. There is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

Subtypes of delirium are based on the type of arousal disturbance:

- Hyperactive
- Hypoactive
- Mixed (both hyper and hypoactivity)

Assessment
Obtain a thorough history to determine the patient's pre-morbid level of functioning, their use of alcohol and illicit substances and the chronology of the onset of the changes in their mental state.

Cognitive assessment tools such as the Abbreviated Mental Test Score should be used to gauge the patient's cognitive state but will not differentiate delirium from other causes of cognitive impairment. The Confusion Assessment Method is the preferred assessment tool according to NICE guidance. Identify any reversible causes: medication, e.g. medicines with anticholinergic side effects such as cyclizine; corticosteroids; infection; biochemical abnormalities; hypoxaemia; and alcohol withdrawal.

Management

- Non-pharmacological measures are the mainstay of treatment and include:
    - Addressing reversible causes
    - Maintaining adequate hydration and nutrition
    - Managing the patient's environment to reduce confusion and distress e.g.
        - Visible clock to aid orientation
        - Encourage family to visit and explain things fully to them
        - Consistent nursing
        - Good lighting during daytime

- Pharmacological interventions:

    - Consider using haloperidol
        - Oral between 500 micrograms and 1.5mg nocte or b.d. with additional doses every four hours as needed
        - SC between 500 micrograms and 1mg; observe for 30-60 minutes and repeat if necessary
        - Review at least every 24 hours and seek further advice from SPC if not working
        - Discontinue within 7 days if symptoms resolve
    - Benzodiazepines should be used with caution due to their tendency to sedate and increase confusion.

PALLIATIVE CARE EMERGENCIES

Metastatic Spinal Cord Compression (MSCC)

Introduction

- Spinal cord compression is a well-recognised complication of metastatic cancer.

- This can be a catastrophic event leading to paralysis below the level of the compression, urinary retention and faecal incontinence.

- If treated early, these problems can usually be prevented or at least partially reversed.

- MSCC and vertebral metastases (VBM) occur more frequently in some tumour types, when there is metastatic disease (especially bone) and in the later stages of a cancer trajectory. Lung, breast and prostate cancers account for over 50% of cases; lymphoma and myeloma account for 20%. Patients at high risk may have been identified by treating clinical teams and informed both of features to look out for and what to do if they suspect that they may be developing VBM or MSCC. Such patients should have been provided with an MSCC information booklet.

- Many of the features of MSCC (back pain, weakness, bladder and bowel changes) are non-specific features of advanced cancer so the patient's symptoms and signs in the 'context' of their cancer must be considered.

- MSCC and VBM can be suspected clinically but can only be proven by imaging (MRI is the gold standard).

- Patients should only be referred for MRI if they are fit enough to tolerate an MRI scan (40 minutes lying flat) and able to travel to the local radiotherapy or spinal surgical unit for treatment if MSCC is confirmed.

- Patients with suspected MSCC should have an MRI within 24 hours.

- Patients with suspected VBM should have an MRI within 7 days.

- Initial MRI imaging will be performed at the patient's local hospital unit and is accessed via the local/regional cancer unit pathway, usually via their Acute Oncology contact point.

Please refer to NICE Clinical Guideline CG75: Metastatic spinal cord compression: diagnosis and management of adults at risk of and with metastatic spinal cord compression.

Symptoms

Symptoms suggestive of spinal metastases:

1. Pain in thoracic or cervical spine
2. Progressive lumbar spinal pain
3. Spinal pain aggravated by straining
4. Localised spinal tenderness
5. Nocturnal spinal pain preventing sleep

Symptoms suggestive of MSCC:

1. Pain

a. Back pain or nerve root pain either unilateral or bilateral, particularly if associated with alteration in gait

b. May be aggravated by movement, coughing or lying flat

c. May precede other symptoms by up to 6 weeks

d. May be absent in approximately 10% of patients

2. Weakness

Motor weakness below the level of the lesion. This may be rapid or slow in onset and can be subtle in the early stages. Descriptions of perceived changes in strength are important.

3. Subjective sensory disturbance

Often precedes objective physical signs, e.g. "I feel like I am walking on cotton wool". Proprioceptive changes may lead to gait dysfunction perceived as 'poor balance'.

4. Bladder/bowel dysfunction.

Urinary retention often develops insidiously and generally occurs late.

Signs

The absence of signs does not exclude early spinal cord compression. Investigations should be considered on the basis of history alone in a patient who is at risk.

- Weakness/paraparesis/paraplegia
- Change in sensation below level of lesion (not always complete loss of sensation)
- Reflexes: absent at level of lesion, increased below the lesion
- Clonus
- Painless bladder distension
- Loss of anal tone

N.B. Sensory and reflex changes may occur secondary to other disease processes or previous neurotoxic chemotherapy.

Investigations and Management

The following general principles apply to the investigation and management of VBM and MSCC.

Investigations

Urgent

- Contact your local cancer unit/Acute Oncology team/spinal surgical team or pathway coordinator as per local policy via their dedicated number to discuss the case and the need for further assessment/evaluation.

- Whole spine MRI - investigation of choice and shows full extent of disease. This should be done within 24 hours if MSCC is suspected.

- Do not use plain radiographs to diagnose or exclude spinal metastases or MSCC.

- If suspected VBM only (i.e. no neurology) then whole spine MRI within 7 days is indicated. Discuss with the patient's Consultant Clinical Oncologist (if they have one), the Consultant Clinical Oncologist linked to the appropriate site-specific MDT (if you do not know who this is contact the site-specific MDT coordinator) or, if all other avenues fail, the Clinical Oncology SpR on-call. Symptomatic VBM is not an emergency in the same way as suspected MSCC.

Management

Corticosteroids can be commenced if there is strong clinical suspicion of cord compression and no contraindications, pending definitive investigations. Give dexamethasone 16mg stat orally, then continue on 16 mg/day until further review. This may give short term improvement while arrangements are being made for investigations and treatment. After surgery or radiotherapy, dexamethasone can be reduced over 5-7 days unless neurological function deteriorates. Monitor blood glucose levels while patient is on corticosteroids (peak levels would be expected in early evening after a morning dose).

Surgery can be appropriate in certain situations. The Clinical Oncology team will undertake appropriate assessment and triage of patient with proven MSCC on MRI. Direct approach to the surgical team for patients with pre-existing proven malignant disease and MSCC should not be undertaken. In most cases surgery should be followed by high dose radiotherapy. Adhere to local policy with regards to referral for radiotherapy or surgery (decompression and spinal stabilisation).

Palliative radiotherapy forms the mainstay of treatment in most cases. The Clinical Oncology team will arrange delivery of this after MRI review and patient triage have been undertaken by them.

Chemotherapy is rarely used in acute management of MSCC but may be indicated in future management as MSCC/VBM reflects a background of progressive cancer.

Active anti-cancer therapy may not be appropriate for patients in the late stages of their cancer trajectory, in those who are unfit for travel, MRI scanning or radiotherapy treatment, or who have established paraparesis and are pain free.

Supportive care: make a full holistic care assessment. Pain relief should be offered to all patients.

Venous thromboembolism prophylaxis should be undertaken following assessment according to local policy.

Rehabilitation: patient positioning and mobilisation should be undertaken according to patient ability/ deficit. Flat bed rest is not routinely advocated and patients may sit inclined as their pain and sitting balance permit. If safely ambulant, this should be encouraged. Patients should have a physiotherapy and/or occupational therapy assessment to agree an initial rehabilitation plan. Aggressive rehabilitation is often not appropriate (as it will be hampered by the progressive background malignancy with fatigue and limited ability to comply) but fitter patients with residual but reduced function, and at an earlier phase of their cancer trajectory, may benefit from onward referral to local rehabilitation teams (though availability of local services may vary).

Superior Vena Caval Obstruction (SVCO)

Introduction

- Most commonly seen in lung cancer (75-80%)
- Can be the presenting feature of lymphoma, particularly in younger patients
- Regard as emergency, as patient's condition may deteriorate rapidly

Symptoms and Signs

1. Breathlessness is the most common symptom (>60%)
2. Swelling or discolouration of the face and neck
3. Feeling of fullness in the head
4. Bending forward or lying flat may aggravate signs and symptoms
5. Non-pulsatile raised jugular venous pulse [JVP]
6. Dilated anterior chest wall and neck veins

Investigations

Discuss with radiologist regarding local policy:

- Chest X-ray - may reveal widened mediastinum or mass
- Thoracic CT scan is the investigation of choice

Management

Vascular stenting is usual treatment of choice although radiotherapy or chemotherapy may be good alternatives.

Chemotherapy may be the treatment of choice in lymphoma and small cell lung carcinoma (if diagnosis previously established). Radiotherapy is useful in patients with SVCO from non-small cell lung carcinoma.

The evidence for the use of corticosteroids as a holding measure before definitive treatment is lacking. Where used this should be for a limited duration. Discussion with local respiratory team/oncologist is recommended.

Recurrent superior vena caval obstruction
Radiotherapy may be considered. Vascular stents may be replaced. Thrombolysis may be considered if a stent is blocked by thrombus.

Outcome

Treatment often gives useful symptomatic relief.
If the SVCO is untreatable, the patient has a prognosis of days.

Hypercalcaemia

Introduction

- Affects approximately 20-30% of patients with advanced cancer
- Most commonly seen in multiple myeloma, breast, and lung (squamous) carcinomas
- Can also occur in lymphoma, leukaemia, renal and prostate cancer
- Consider in unexplained nausea, vomiting, confusion or constipation
- More commonly due to tumour secretion of parathyroid hormone-related protein rather than bone metastases
- May develop insidiously
- Cancer is usually advanced if hypercalcaemia develops

Symptoms and Signs

Severity of symptoms is more related to the speed of rise of the serum calcium rather than the absolute level.

- Non-specific early symptoms: lethargy, malaise, anorexia
- Common symptoms: nausea and confusion
- Other symptoms: constipation, thirst and dehydration
- Late features: drowsiness, fits, coma

Investigations

- Corrected serum calcium
- Urea and electrolytes

Management

Treat if serum calcium is elevated, the patient is symptomatic and it is clinically appropriate.

- Pre and post dose rehydration with 0.9% sodium chloride tailored to the patient's renal function, cardiovascular status and oral intake.
- Intravenous bisphosphonate, e.g. zoledronic acid 4mg IV is the agent of choice. Pamidronate 90mg, or ibandronate between 2 to 4mg are other options. Choice and dose depends on local guidelines and the patient's renal function.

Follow Up

Recheck calcium if symptoms have not improved after 3-4 days.

- Maximal response to bisphosphonates is seen after 6-11 days.
- If appropriate, repeat or give a different

bisphosphonate if calcium level has not decreased.

- Consider investigating for hyperparathyroidism in selected patients.
- For recurrent hypercalcaemia consider intermittent intravenous bisphosphonates. If repeated doses of bisphosphonates are anticipated, patients should have a dental assessment and their dental practice informed, to minimise the risk of osteonecrosis of the jaw.

Outcome

- Average duration of response is 3-4 weeks.
- Patients should be informed that hypercalcaemia may recur and to monitor for symptoms.
- Prognosis depends on the underlying pathology, but refractory hypercalcaemia is a poor prognostic indicator.

LYMPHOEDEMA

Introduction

Lymphoedema occurs due to the inability of the lymphatic system to maintain normal tissue homeostasis. This results in an accumulation of protein-rich fluid in the subcutaneous tissues. Lymphoedema is one form of chronic oedema. In patients with cancer, lymphoedema is usually secondary to the underlying cancer or previous cancer treatment.

Characteristic Features

- Oedema
- Chronic inflammation
- Skin changes, e.g. dry skin, thickened tissues (Stemmer's sign)
- Heaviness and aching in the affected limb
- Excess fibrosis
- In early lymphoedema pitting is demonstrated
- With time, this feature is lost due to the oedema having a high protein content

General Management

Where available, patients should be referred to specialist lymphoedema clinics.

The core treatment elements are:

- Skin care - keep skin clean and moisturised with non-perfumed emollient (e.g., Diprobase®, Doublebase® or Zerobase®) or aqueous cream
- Compression/support
- Movement and exercise
- Simple lymph drainage, self-massage techniques

Avoid affected limb for any medical procedure, e.g. injection, venepuncture, blood pressure measurement.

Management of Cellulitis in Lymphoedema

Comprehensive advice is available in the consensus document from the Lymphoedema Support Network and British Lymphology Society (www.thebls.com, April 2015).

Treat early, monitor closely and continue antibiotics for at least 14 days after clinical improvement is observed.

1. Oral amoxicillin 500mg t.d.s. (clarithromycin 500mg b.d. or erythromycin 500mg q.d.s. if penicillin allergic).
2. If evidence of Staphylococcus aureus infection, e.g. folliculitis, pus formation or crusted dermatitis, add or substitute flucloxacillin 500mg q.d.s.
3. Follow guidance on the British Lymphology website, www.thebls.com.

Acute infection is usually painful; review analgesics. Avoid compression garments and NSAIDs in acute attack. If the patient develops systemic symptoms, IV antibiotics may be required; seek specialist advice.

Recurrent cellulitis

Antibiotic prophylaxis is needed if the patient has had 2 or more attacks of cellulitis per year. Penicillin V 500mg daily (erythromycin 500mg daily if penicillin allergic) first line. Consult www.thebls.com and refer for specialist advice.

Further information

The Lymphoedema Support Network: www.lymphoedema.org/lsn The British Lymphology Society: www.thebls.com

MOUTH CARE

General Mouth Care

Ensure that the patient is asked about mouth problems and that the mouth is examined.

- Use of a small soft tooth brush is preferable for mouth care. Foam mouth swabs are an alternative. Check the foam head is firmly attached. Do not leave swabs soaking because of risk of detachment and choking. Dispose after single use.
- Remove dentures at night. Clean by using a denture brush and soak in water overnight.
- If the patient is conscious, support them to brush teeth. Perform mouth care at least twice a day.
- If patient is unconscious, provide mouth care hourly using water to clean teeth, gums, tongue and mouth.

Dry Mouth

Continue essential mouth care and look for reversible causes. Review medications; patients are often on multiple medicines which can cause dry mouth.

Suggestions:

- Frequent sips of cold unsweetened drink
- Sugar-free chewing gum/low sugar pastilles/boiled sweets
- Topical artificial saliva substitutes: Biotene Oral-balance®/AS Saliva Orthana® (contains pork)
- If the above measures are not effective, salivary stimulants may be an option; seek specialist advice

Coated Tongue

This indicates poor salivary gland function. Continue essential mouth care management and address dry mouth.

- Brush tongue gently with a soft small tooth brush.
- Pineapple is sometimes suggested, but caution is suggested with the use of acidic substances, as they can increase risk of dental caries/infections. The importance of this depends on the person's prognosis and whether they still have teeth.

Sore or Ulcerated Mouth

Continue essential mouth care management and address dry mouth. Identify the cause and treat where possible. Sore mouth can be caused by infection, mucositis post-chemo or radiotherapy (see local guidelines), by tumour, by aphthous ulcers or by vitamin deficiency.

Suggestions:

- If conscious and able to spit out, consider use of Gelclair® alcohol free mouthwash or normal saline.
- Topical analgesia options: paracetamol mouth rinse, benzydamine hydrochloride (Difflam®), choline salicylate (Bonjela®)
- If not responsive to the above measures, consider use of topical anaesthetics and apply directly to painful area, e.g. lidocaine (Xylocaine®) 10% spray applied using cotton bud p.r.n. Avoid anaesthesia to pharynx before meals/drinks.
- For severe oral pain, consider the combined use of topical and systemic preparations. Seek specialist advice.

Oral Candidiasis

Continue essential mouth care management.
Can present as a dry mouth, loss of taste, reddened tongue, soreness, dysphagia, angular cheilitis and asymptomatic.

Look for and treat reversible causes: immunosuppression, steroid use (oral/inhaled), dry mouth, dehydration, poor oral hygiene, mucosal damage.

- Consult local guidelines for use of antifungals/ check for drug interactions. Options include: nystatin oral suspension 100,000 units/ml, 5mL q.d.s. for 7 days; hold in mouth for 1 minute, then swallow (avoid concomitant use of chlorhexidine) or fluconazole (capsules or suspension) 50mg daily for 7 days. (May need higher doses/longer courses for immunosuppressed patients).
- Remove and clean dentures (cleansing agent depends on the dentures).
- Taste disturbance can improve with essential mouth care management, addressing dry mouth and infection. Maintain nutrition where possible and refer to a dietician.

THE LAST DAYS OF LIFE

Recognition of imminent death is important. It allows withdrawal of unnecessary treatments and preparation of the patient and family/carers for death. This phase is often heralded by a more rapid deterioration in the patient's general condition. It can be difficult to recognise. Consider if there are any potentially reversible causes for the patient's condition, e.g. infection, opioid toxicity, metabolic abnormalities (uraemia, hypercalcaemia) and if it is appropriate to manage these. In a patient with an advanced illness the following symptoms and signs may indicate that the prognosis is short:

- Profound weakness
- Confined to bed for most of the day
- Drowsy for extended periods
- Disorientated
- Severely limited attention span
- Loss of interest in food and drink
- Too weak to swallow medication.

Actions

1. Sensitively check the awareness of patient and family/carers and explain the plan of care.

2. Negotiate appropriate treatment and advance care plans with the patient, if they have capacity. Check if an Advance Decision to Refuse Treatment (ADRT) has been made or a Lasting Power of Attorney (LPA) for welfare appointed.

3. If the patient does not have capacity, clinical decisions must be made in the patient's best interests in line with the Mental Capacity Act.

Family, carers and other healthcare professionals should be consulted. The role of the family is to advise on what the patient would have wanted for him/herself.

4. Establish the patient's preferred place of care and preferred place of death. This should take into account the needs and wishes of the patient and the family/carers.

5. Fast Track/Continuing Care Funding Form or equivalent needs to be signed for patients wishing to be cared for in a home or care home setting.

6. CPR status should be reviewed. In accordance with local policy, complete a transferable regional DNACPR form. Always try and discuss this with the patient, their families and carers.

7. If at home/care home ensure an Out of Hours Handover Form has been completed and the record/notes updated as per local policy, e.g. EPaCCS/local register/single point of access.

8. Ensure that the patient and family/carers have the telephone numbers for NHS 111, out of hours palliative care line, locally available services, the community palliative care team, local hospice and their own GP and district nursing team.

9. Professional carers may need to acknowledge and share their own feelings. Mutual support and teamwork are important.

10. Ensure all anticipatory medications are sent home with the patient if being discharged from a hospital or other place of care. This ensures the patient does not have to wait for medication if they start to develop symptoms.

11. Ensure all individuals involved in the patient's care are aware of their condition, such as GPs, district nurses, local hospices and community palliative care teams.

12. Ensure regular review by nursing and medical staff, including night care, as agreed with the patient and their family.

13. When the patient is in the last days/hours of life support with an individualised care plan as per local policy.

Physical Care
Care and support

1. If a patient is to be discharged home from hospital to die, ensure the general practitioner, district nurse and where appropriate, the community palliative care team are aware.

2. Adequate day and night nursing support needs to be arranged. Consider night sitters.

3. Involve family/carers in practical care as much as they wish and discuss the plan of care.

Priorities of care include:

- Assess regularly for common symptoms at the end of life: pain, agitation, respiratory secretions, nausea and vomiting and breathlessness.
- Treat dry mouth with good and regular mouth care.
- Immobility and pressure areas - bed, mattress, positioning needs to be assessed.
- Continence - consider catheter, convene or pads and monitor for signs of retention.
- Bowel care - assess for bowel problems that may cause discomfort, such as constipation or diarrhoea.
- Assess the psychological, religious, cultural and spiritual care needs of the patient and family.

Hydration and nutrition

A reduced need for food and fluids is part of the normal dying process and patients should be supported to take food and fluids by mouth for as long as tolerated. Symptoms of thirst/dry mouth are often due to mouth breathing or medication/oxygen therapy and good mouth care is essential.

For many patients, the use of clinically assisted (artificial) hydration will not be of benefit and decisions about their use should be made in a patient's best interests. If clinically assisted artificial hydration or nutritional support is in place, review rate/volume/route according to individual need. The possible benefits of withdrawing or reducing clinically assisted hydration/nutrition include reduced vomiting and incontinence, reduced painful venepuncture. If indicated, fluids can be administered subcutaneously; monitor for uncomfortable fluid accumulation at the infusion site.

Medications
Reassess the indications and potential benefits in the context of the terminal phase for ALL medications. Only continue medication needed for symptom management. If the oral route is not appropriate the subcutaneous, transdermal or rectal routes can be used for many symptom management drugs.

When in the last hours/days of life refer to local symptom management guidelines where available. Ensure anticipatory medications are prescribed and available for the common symptoms which may develop in the last hours or days of life: pain, terminal restlessness, respiratory tract secretions, breathlessness, nausea and vomiting.

Terminal restlessness
Assess the patient carefully. Restlessness can occur at the end of life but there may be a precipitant, therefore look for evidence of:

- Physical discomfort - pain related to the underlying condition, urinary retention, faecal impaction or new event, e.g. haemorrhage, malfunctioning syringe pump.
- Respiratory distress - breathlessness, cough, tracheal obstruction.
- Neurological problems - fits, hallucinations, myoclonic jerks, motor restlessness. Remember these may be caused by medicines (including opioids and anti-emetics).
- Psychological distress (see below).
- Delirium.

If there are no reversible precipitating factors or psychosis/delirium, midazolam is the drug of choice

(see syringe pump section, page 74). After non-pharmacological measures, haloperidol is indicated for delirium. If midazolam alone is not effective consider adding haloperidol or levomepromazine.

Respiratory tract secretions or 'Death Rattle'
This is a rattling noise produced by the movement of secretions in the upper airways in patients who are too weak to expectorate effectively. Relatives and carers may find this distressing. It is important to explain to the relatives/carers that this is unlikely to be causing distress to the patient.

- Repositioning of the patient and postural drainage may help
- Anti-secretory drugs can be used (see syringe pump section or local symptom management guidelines)
- Prompt drug treatment is required

For resistant symptoms consider other causes, e.g. gastric or chest secretions and manage accordingly.

Distressing terminal events
Events such as haemorrhage, fits or tracheal obstruction are unusual and can often be anticipated and a management plan discussed with nursing staff in advance. Prescribe appropriate p.r.n. medication, e.g. midazolam, to relieve distress and to sedate if necessary. Seek advice from palliative care team if unsure. If possible, try and discuss the possibility of such events with family or carers if they are thought to be more likely, e.g. known head and neck tumours near major vessels. This may allow for better preparation if such an event were to happen.

Do not attempt cardiopulmonary resuscitation (DNACPR) decisions

If a patient is in the last days of life, cardiopulmonary resuscitation (CPR) will not be of clinical benefit. The resuscitation status of the patient should be discussed within the clinical team and documented as per local policy. It is good practice to explain to the patient and their carers: why CPR will not be attempted; that the focus of care is on palliation and comfort; and in the home setting, to ensure that family members know what to do when the patient dies.

Advise them to keep the DNACPR form somewhere safe so that it can be shown to all healthcare providers. https://www.resus.org.uk/dnacpr/decisions-relating-to-cpr/

Psychological and spiritual care of patient and family

The patient, relative and carer should be given the opportunity to discuss what is important to them at this time. Decisions about the plan of care should be communicated to the patient where appropriate and to the relative or carer. The patient may be anxious for themselves or others and addressing psychological and spiritual needs may contribute to alleviating symptoms of agitation.

Consider barriers to communication such as hearing, vision and speech difficulties, learning disabilities, dementia, neurological conditions, language barriers and confusion. The relative or carer may know how specific signs indicate distress if the patient is unable to articulate their own concerns.

Encourage open communication and explore fears and concerns:

- Facilitate expression of emotions
- Involve children and those with learning disabilities
- Remember spiritual care and religious needs (offer to contact chaplain, priest, rabbi etc. if appropriate)
- Consider music, art, poetry, reading, photographs or something else that has been important to the well-being of the patient

Care After Death

Practical and legal aspects to attend to after death

Arrangements may vary depending on place of death and local bereavement service provision.

- Inform relatives when referral to the Coroner might be necessary, e.g. mesothelioma. It is preferable to do this before the patient's death.
- Ensure prompt verification of death, personal care after death and provision of death certificate.
- Provide information about the role of the undertaker and how to register a death.
- For deaths not occurring in the patient's own home, ensure patient's GP is informed within 24 hours.
- For deaths occurring at home, ensure planned visits are cancelled and arrangements made to return equipment.
- Ensure hospital appointments (and transport) are cancelled and hospitals/consultants involved with the patient's care are informed.

Bereavement

It is good practice when someone has died, to provide written information about the common feelings of grief and available support, and to identify those at increased risk in bereavement. Risk factors include:

- previous multiple losses or recent losses
- ambivalent relationship
- dependent children involved
- bereaved parent
- previous psychological or psychiatric problems or substance abuse
- people living alone or feeling unsupported

Seek advice from colleagues and the relative's GP, with their permission, if one or more of these risk factors are present.

It is good practice to review how someone is coping 6-8 weeks after the death.

SYMPTOMS IN DEMENTIA

Assessment – General

The following considerations are particularly important when assessing a person with dementia:

- If the patient cannot self-report symptoms including pain, involve other people who know them, e.g. family members, professional carers, other clinicians, in order to better understand their 'normal state' and usual distress behaviours. Changes in behaviour can then be understood in context as they may indicate unrelieved symptoms.

- Consider using "This Is Me" or similar to ensure a patient's history and preferences are recorded and shared with staff.

- Use supportive communication strategies: ask short questions; allow additional response time; use gestures; minimise distractions/external noise; address sensory impairments; seek confirmation of assumptions made.

- Does the patient have the mental capacity to consent, with support, to examination/ investigation/taking medications? Will investigation alter management or can you treat on a presumed diagnosis?

Distress and Pain Assessment

Patients with dementia are less likely to ask for and receive pain relief. Pain assessment should include patient self-report, physical examination, caregiver reports and behavioural observations.

Several tools are available to support pain assessment in people with cognitive impairment, including PAIN-AD, Abbey Pain Scale and DISDAT. When using these tools, watch for over-identification of pain when the person is actually distressed by other causes. Signs of distress may include: agitation, wandering, withdrawal, night-time waking, not eating/drinking.

Patients may be unable to communicate their experience of pain because of impaired memory or lack of expressive language. Ask about their pain using descriptive words such as aching, hurting, sore. Focus on current pain and ensure assessment is made during periods of activity and of rest. Consider using different representations of pain to help people self-report, e.g. visual, numerical and verbal rating scales. Select an appropriate tool for the individual and teach them how to use it when their pain is least severe.

Medication Use – General

- Is the person compliant with their medication?

- People with dementia are vulnerable to the side effects of medicines that exacerbate confusion, e.g. anticholinergics, amitriptyline.

- In Parkinson's dementia and Lewy Body dementia, dopamine antagonists can cause confusion, hallucinations and delusions.

- Use oral medication as first line wherever possible. Other formulations, e.g. transdermal patches may be useful.

Nausea and Vomiting

In addition to the medicine management approaches outlined on page 30, the following considerations are important:

- Treat reversible causes where appropriate, e.g. infection, drug side-effects.

- Are environmental factors contributing? Can they be minimised, e.g. by reducing strong food smells, offering smaller portion sizes?

- Consider longer acting anti-emetics to reduce tablet burden.

Dysphagia

Swallowing problems, loss of appetite and weight loss are common issues, especially as the severity of illness increases. Comfort feeding small amounts of appropriately thickened foods may provide enjoyment of eating and alleviation of hunger or thirst.

Neuropsychiatric Symptoms

These are nearly universal in dementia and agitation is among the most distressing for patients and family carers. Exclude or treat specific causes, e.g. pain, and prioritise non-pharmacological approaches.

Delirium is extremely common in patients with advanced dementia, potentially exacerbated by dehydration, and often unrecognised or misdiagnosed as worsening dementia, depression, anxiety or psychosis.

Obtain a thorough history to determine the patient's pre-morbid level of functioning, the onset of changes in

their mental state and any potential cause, e.g. infection, medication. Whilst antipsychotics may be necessary, all psychotropics including benzodiazepines can increase confusion and should be used with caution.

Occasionally in severe anxiety/agitation at the end of life a trial of a benzodiazepine or antipsychotic may be appropriate, weighing up the risks and benefits. Antipsychotics should be avoided if possible in Lewy body dementia as these can cause severe side effects.

SYRINGE PUMP PRINCIPLES

In palliative care a syringe pump or driver is a way of administering medication continuously via the subcutaneous route when the patient is unable to swallow or absorb oral drugs due to:

- Persistent vomiting, intestinal obstruction, dysphagia, weakness, unconsciousness or mouth, throat and oesophageal lesions.

Where indicated, syringe pumps can be used for a short period for symptom control, or for longer in the terminal phase. The rationale for use should be explained to the patient and their relatives.

Considerations:

- Doses of medication are calculated on the basis of patients' previous requirements

- Following commencement of a syringe pump it will be several hours before therapeutic levels are achieved, so consider giving a stat dose of medication equivalent to the normal breakthrough/ p.r.n. dose

- Syringe pumps require careful monitoring and should be prescribed on prescription/syringe pump charts as per local syringe pump policies

- Inadequate pain control is not an indication for syringe pump use unless there is reason to believe oral medications are not being absorbed or the patient has nausea or vomiting

- Recommended sites for insertion of the subcutaneous cannula are the anterior chest wall, upper arms, abdominal wall and thighs

NOTE:
A variety of models of ambulatory infusion devices (syringe pumps) are in use. Graseby ambulatory syringe pumps no longer meet MHRA safety requirements and are being phased out. As a result, McKinley T34 syringe pumps are now widely used in the region. Alternative MHRA approved syringe pumps may also be available. Please follow your local syringe pump policy.

COMMON MEDICINE DOSAGES FOR SUBCUTANEOUS MEDICATIONS & INFUSIONS

All the medicines on the following two pages (76-77) can be given as subcutaneous infusions in a syringe pump.

Remember to prescribe subcutaneous p.r.n. medication. If using more than one drug in a syringe pump, check compatibilities with current PCF, pharmacy, or Specialist Palliative Care Team.

To convert from oral morphine see section 1.2.1. For other opioids, seek specialist advice. If symptoms are not controlled, other regimens may be needed. Seek specialist advice.

Commonly used sub-cutaneous medications	Usual starting p.r.n. dose (and frequency)	Usual 24 hour dose range	Usual ampoule size information	Comments
PAIN AND BREATHLESSNESS				
Diamorphine / Morphine	1 to 2.5mg sc p.r.n for opioid naive 1/6th of the 24 hour SC dose	Between 5 and10mg/24 hours if opioid naïve. For diamorphine: 1/3 of previous 24 hour oral morphine dose/24 hours CSCI. For morphine: 1/3 to 1/2 of previous 24 hour oral morphine dose/24 hours CSCI. See local guidelines. Seek advice.	Diamorphine: 5mg, 10mg, 30mg, 100mg, 500mg Morphine sulphate: 10mg/1ml, 15mg/1ml, 20mg/1ml, 30mg/1ml, 20mg/2ml, 30mg/2ml, 40mg/2ml, 60mg/2ml	Seek advice if: o patient requiring rapidly escalating doses o patient in renal failure
NAUSEA AND VOMITING				
Haloperidol	500 micrograms	1 to 5mg/24 hours CSCI	5mg/1ml	Haloperidol has anxiolytic and sedative properties
Cyclizine	50mg (max t.d.s.)	150mg CSCI (max dose)	50mg/1ml	Incompatible with hyoscine butylbromide
Metoclopramide	10mg (max t.d.s.)	30 to 60mg/24 hours CSCI	10mg/2ml	Prokinetic effect antagonised by cyclizine
Levomepromazine	6.25mg	6.25mg to 25mg/24 hours CSCI	25mg/1ml	Can be sedating

RESPIRATORY SECRETIONS - Early intervention for "death rattle" is required				
Hyoscine butylbromide (Buscopan®)	20mg	Between 60 to 120mg/24 hours CSCI	20mg/1ml	Not sedating Can be incompatible with cyclizine
Glycopyrronium	400 micrograms	600 micrograms to1.2mg/24 hours CSCI	200 micrograms/1ml, 600 microgram/3ml	Not sedating
Hyoscine hydrobromide	400 micrograms	1.2 to 2.0mg (max dose 2.4mg/24 hours) CSCI	400 micrograms/1ml, 600 micrograms/1ml	Can be sedating (use other anti-secretory drugs 1st line)
AGITATION - Consider Haloperidol if patient is suffering from agitation and delirium				
Midazolam	2 to 5mg	10mg to 20mg/24 hours CSCI (starting dose). May be increased to 60mg/24 hours according to response. Seek SPCT advice.	10mg/2ml. Other preparations are available, store separately	Muscle relaxant, anxiolytic and anticonvulsant (see below). If ineffective seek specialist advice.
Haloperidol	500 micrograms	1 to 5mg/24hours CSCI	5mg/1ml	Haloperidol has anxiolytic and sedative properties
ANTICONVULSANT				
Midazolam	10mg	20 to 60mg/24 hours CSCI to replace oral anti-convulsants may be required.	10mg/2ml. Store high and low strength midazolam separately.	Seek SPCT advice re management of prolonged fits.

Yorkshire and Humber Palliative and End of Life Care Groups

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